IS SELECTION OR MUTATION THE MORE IMPORTANT AGENCY IN EVOLUTION?

By Professor WILLIAM E. CASTLE
BUSSEY INSTITUTION

THIRTY years ago the opinion prevailed among biologists that biological evolution, like geological, is a very gradual process in which agencies acting with uniformity over long periods of time gradually produce changes in existing species through natural selection. About the year 1900 a change of opinion set in, which may be described as a tendency to return to the older idea of the sudden and special creation of species. Not that the idea of evolution was to be abandoned, but the province of natural selection was now thought to be less extensive, its action being limited to deciding what species shall survive. As to the *origin* of species, this was supposed to occur suddenly as a result of undetermined agencies, but not to be either attended by natural selection or caused by it. This theory of the sudden and spontaneous origin of species unattended by natural selection is known as the mutation theory. Philosophically it has much in common with those geological theories which regard geological epochs as inaugurated by terrestrial catastrophes, and those astronomical theories which involve cosmic collisions and explosions in the origin of new heavenly bodies. Historically the mutation theory owes its present popularity chiefly to the work of the Dutch botanist, DeVries, and the Danish botanist, Johannsen, though many others have given it ardent and valuable support.

In clearing the ground for a theory that species are not produced by natural selection, DeVries and Johannsen have attempted first to show the inability of selection of any sort to produce specific changes. Selection, they maintain, can produce nothing new. It can only sort over and rearrange variations already present. The strongest existing evidence in favor of this view consists of the selection experiments of Johannsen with size variations in beans and the similar experiments of Jennings with paramecium. As a result of this and other similar work a useful classification of variations has been established, which are said to be either *phenotypic* or *genotypic*. The former are variations due to purely environmental causes, such as soil, temperature, humidity, food, etc. These are not inherited. They are apparent rather than real racial changes so far as evolution is concerned. In contrast to these phenotypic variations are those called genotypic, the causes of which lie in changes within the germinal substance. They are hereditary.

Environmental agencies, those which produce phenotypic variation, are very complex and oftentimes one agency counteracts another. The

resultant or combined action of several independent agencies is in biology as elsewhere, to produce variation of the frequency-of-error sort. This kind of variation which mathematicians express in the so-called "normal" curve or "curve-of-error" biologists call "continuous" because it consists of graded quantitative variations which shade insensibly into each other.

The best known cases of genotypic or heritable variations are those which are of considerable magnitude and in which a single genetic factor is involved, because it is easier to follow the history of these from generation to generation. It was therefore a natural but none the less unfortunate conclusion on the part of the mutationists that *all* continuous or graded variations are phenotypic (not inherited), while all genetic (heriditary) variations are discontinuous. Manifestly this is a pure assumption, for logically it is to be expected that several independent genetic agencies acting simultaneously will produce continuous variation, whereas a single and isolated environmental change may produce discontinuous variation. In fact, Mendelian studies have already shown that several independent genetic factors may frequently produce a series of graded or continuous variations. But if these supposed factors are themselves constant, it is theoretically possible to alter the racial type by selection only to a limited extent. For the action of selection will be restricted to the production of the possible combinations or permutations of the genetic factors present. But if, on the other hand, genetic factors are themselves variable in a quantitative way, continuous or graded variation of the organism might result from the action of one genetic factor alone, and all the more from the joint action of several such varying factors. In that case selection would be capable of producing uninterrupted change in racial characters, because it could not only isolate particular combinations of genetic factors, but it could also isolate higher or lower quantitative stages of each factor. Its action would therefore be limited only by the limits of variability of each genetic factor.

Mendelians have generally assumed that the genetic factors with which they are concerned are quantitatively invariable. This assumption was made, probably at first, for logical simplicity and then from habit, so that now it has come to be one of the fundamental tenets of many Mendelians. But so far as evidence is concerned, either observational or experimental, it has small basis. At first Mendelians assumed that all *characters* which Mendelize are invariable, that crossing does not affect a Mendelian character, that the recessive character when it is recovered again following a cross is the same as ever and so Bateson proposed in 1902 to discard old ideas of racial purity and institute a new test of racial purity which should consist simply in determining the presence or absence of particular Mendelian characters. But more careful study of Mendelian characters soon showed that they were not

invariable. Extracted recessives were frequently observed to be different from the recessives which entered into a cross two generations previously. So the idea of character constancy had to be abandoned, but in its place has come the idea of *factor* constancy. It is now held by many that the changes observed in Mendelian characters as a result of crossing are due to other independent genetic factors introduced by the cross, the main factors themselves being unaffected. If this is so, then by eliminating these *other* or modifying factors it should be possible to secure an invariable or pure race. Such pure races it was believed by Johannsen that he had secured in the case of self-fertilized beans studied by him, and Jennings at one time entertained similar views concerning asexually produced races of paramecium. But it should be pointed out that in neither case was a Mendelian character under observation, so that these investigations have no direct bearing on the question whether Mendelian factors are or are not quantitatively variable.

In my studies of Mendelian heredity I early encountered characters obviously variable and I have been engaged for several years in trying to discover the causes of this variability. Crossing was evidently such a cause, contrary to the earlier idea of character constancy and gametic purity. This having been settled, attention was next directed to the theory of factor constancy. To test this, crossing must obviously be avoided, since by this means the experimenter might unwittingly introduce modifying factors. Modifying factors must either be eliminated or rendered constant before one could hope to test the variability or invariability of a single factor. The surest means to this end would be inbreeding attended by selection. Under this procedure modifying factors should be gradually eliminated or rendered constant (homozygous) and a condition of racial stability secured equal to the stability of the single genetic factor concerned in producing the character under observation.

If the genetic factor in question were entirely stable and invariable, racial change under selection should gradually slow up and finally stop altogether, as one modifying factor after another was eliminated or rendered constant (homozygous), and this is what DeVries and Johannsen have assumed actually occurs.

The best material which I have been able to discover on which to test this matter consisted of piebald black-and-white or gray-and-white hooded rats. This color pattern of white and pigmented areas behaves in heredity as a simple Mendelian recessive character. (See Fig. 1). It is the alternative (or allelomorph) of the entirely pigmented or "self" condition of wild rats. In crosses with such wild rats the hooded character is recovered as an extracted recessive character in one fourth of the second generation offspring. In a total of 1,483 such offspring, 493, or 24.9 per cent., have been hooded. Individuals possessing the recovered

character frequently have either more or less extensively pigmented bodies than their hooded grandparent and are not entirely uniform among themselves. In fact a family of hooded rats is never entirely uniform, no matter how closely selected and inbred. They produce only hooded young when mated with each other, but some possess rela-

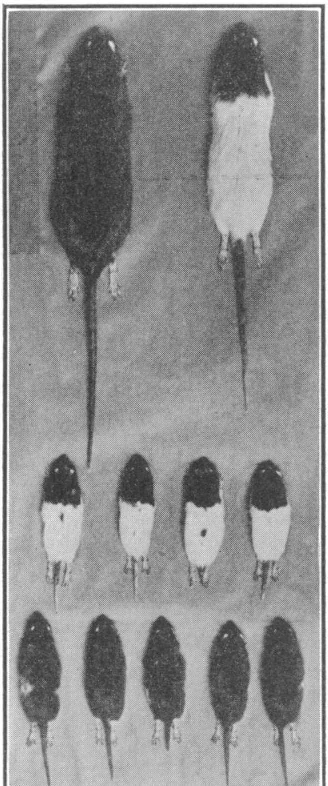

FIG. 1. SKINS OF A LITTER OF NINE RATS AND OF THEIR PARENTS. The inheritance is alternative (Mendelian) but each alternative condition shows slight quantitative variations.

tively more white than others. In order to learn whether these quantitative differences in the hooded character are hereditary, selection experiments were begun in 1907 upon a small colony of hooded rats derived originally from less than a dozen individuals. The blackest rats (*i. e.,* those with most extensive black areas) were chosen to start a plus selection series, and the whitest rats (*i. e.,* those with least extensive black areas) were chosen to start a minus selection series. From the offspring of the plus selected parents the blackest were again chosen, and from the offspring of the minus selected parents the whitest were chosen, and this process was repeated in each generation. Sixteen successive selections have thus far been made in the plus series,

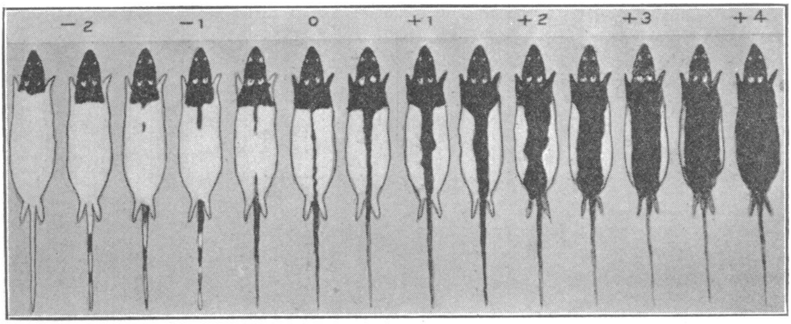

FIG. 2. A SCALE OF ARBITRARY GRADES USED IN CLASSIFYING THE FLUCTUATING VARIATIONS OF HOODED RATS.

and seventeen in the minus series. The plus series has become steadily darker, the minus series lighter, until two very distinct races have resulted. In order to classify the young more accurately and to express in more definite terms the quantitative changes which have taken place in the hooded character, each rat has been graded in terms of an arbitrary scale of increased (plus) or decreased (minus) pigmentation as compared with the original modal condition of the race (zero condition). See Fig. 2.

TABLE I

RESULTS OF THE PLUS SELECTION OF HOODED RATS CONTINUED THROUGH SIXTEEN SUCCESSIVE GENERATIONS

Generation	Mean Grade of Parents	Mean Grade of Offspring	Lowest Grade of Offspring	Highest Grade of Offspring	Standard Deviation of Offspring	Number of Offspring
1	2.51	2.05	+1.00	+3.00	.54	150
2	2.52	1.92	−1.00	+3.75	.73	471
3	2.73	2.51	+ .75	+4.00	.53	341
4	3.09	2.73	+ .75	+3.75	.47	444
5	3.33	2.90	+ .75	+4.25	.50	610
6	3.52	3.11	+1.50	+4.50	.49	861
7	3.56	3.20	+1.50	+4.75	.55	1,077
8	3.75	3.48	+1.75	+4.50	.44	1,408
9	3.78	3.54	+1.75	+4.50	.35	1,322
10	3.88	3.73	+2.25	+5.00	.36	776
11	3.98	3.78	+2.75	+5.00	.29	697
12	4.10	3.92	+2.25	+5.25	.31	682
13	4.13	3.94	+2.75	+5.25	.34	529
14	4.14	4.01	+2.75	+5.50	.34	1,359
15	4.38	4.07	+2.50	+5.50	.29	3,690
16	4.45	4.13	+3.25	+5.87	.29	1,690
						16,107

The first plus selected parents were of mean grade + 2.51. They produced 150 young of somewhat lower average grade than their parents, viz., + 2.05 (see Table I.). A second selection gave a similar result, but with young of slightly lower mean grade, viz., + 1.92. With each subsequent selection it was possible to raise the standard of the selected parents, and in each case the grade of the offspring has in-

creased correspondingly. As a result of the sixteenth selection, 1,690 young have been obtained *every one of which is darker* than *any* hooded rat born in the series previous to the second selection. Accordingly the character of the entire race has changed under selection. This change has come about gradually. Generation by generation, as the mean grade of the parents has advanced, that of the offspring has advanced in like measure, but always lagging behind the grade of the parents. With advance in the *mean* grade of the offspring has gone advance in both the upper and the lower limits of their variation. The amount of variability of each generation of offspring as measured by its standard deviation has decreased to about three fifths of its original extent, but has not changed materially in the last eight or ten generations, and there is no prospect of its declining further. The rate of racial change has also not become less. Reversed selection returns the race toward its previous condition at about the same rate as the departure has taken place.

It seems clear from these observations that the hooded character, though itself a simple Mendelian unit in heredity, is subject constantly to slight quantitative variations which are themselves to some extent hereditary. These quantitative variations are grouped like continuous variations round a mean the position of which may be altered gradually but permanently by repeated selection.

A series of seventeen minus selections yielded results similar to those obtained in the plus selection series, but with a movement of the mean and of the upper and lower limits of variation in the opposite direction (see Table II.). In this case a race has been secured whiter in nearly every individual than any rats contained within the original race. The whitest rats have only a few pigmented spots left on the body, chiefly located on either side of the head close about the eyes, ears and nose. In the plus selected series the blackest rat obtained (grade $+5.87$) was black all over except for the presence of a few white hairs on the chest between the front legs. No fancier would have thought of including it among "hooded" rats, or even among "Irish" (white-bellied) rats; fanciers would undoubtedly have classed it among "self" rats. There is apparently no limit to the quantitative change which can be produced in the hooded pattern by selection, short of its complete extinction in the all white or all black condition toward which our minus and plus selections respectively are steadily tending. Yet there can be no doubt that only a single genetic factor is here involved. A tentatively adopted hypothesis that modifying factors were concerned in it has been definitely disproved. Any finite number of such modifiers would have been greatly reduced or eliminated altogether by seventeen successive selections, yet no slowing up is observable in the rate of change of the racial character under selection either plus or minus. The changes effected by selection show per-

manency under crosses with wild rats. They change no more nor less than an unselected hooded race does. A first cross of the selected races seemed to show a partial undoing of the changes produced by selection, but a second cross made on a still larger scale, involving over 1,000 second generation individuals, showed no further change of this sort, but instead a return to about what the selected race would have been had no crossing at all occurred.

TABLE II

RESULTS OF THE MINUS SELECTION OF HOODED RATS CONTINUED THROUGH SEVENTEEN SUCCESSIVE GENERATIONS

Generation	Mean Grade of Parents	Mean Grade of Offspring	Lowest Grade of Offspring	Highest Grade of Offspring	Standard Deviation of Offspring	Number of Offspring
1	−1.46	−1.00	+ .25	−2.00	.51	55
2	−1.41	−1.07	+ .50	−2.00	.49	132
3	−1.56	−1.18	0	−2.00	.48	195
4	−1.69	−1.28	+ .50	−2.25	.46	329
5	−1.73	−1.41	0	−2.50	.50	701
6	−1.86	−1.56	0	−2.50	.44	1,252
7	−2.01	−1.73	0	−2.75	.35	1,680
8	−2.05	−1.80	0	−2.75	.28	1,726
9	−2.11	−1.92	− .50	−2.75	.28	1,591
10	−2.18	−2.01	−1.00	−3.25	.24	1,451
11	−2.30	−2.15	−1.00	−3.50	.35	984
12	−2.44	−2.23	−1.00	−3.50	.37	1,037
13	−2.48	−2.39	−1.75	−3.50	.34	1,006
14	−2.64	−2.48	−1.00	−3.50	.30	717
15	−2.65	−2.54	−1.75	−3.50	.29	1,438
16	−2.79	−2.63	−1.00	−4.00	.27	1,980
17	−2.86	−2.70	−1.75	−4.25	.28	868
						17,142

The conclusion seems unavoidable that the single genetic factor involved in this case has undergone quantitative change under the influence of selection. If so, two foundation postulates of the mutation theory are false, viz., (1) that continuous or graded variations are not concerned in evolution and (2) that selection of such variations, no matter how long continued, can effect no permanent or progressive racial changes. Selection, as an agency in evolution, must then be restored to the important place which it held in Darwin's estimation, an agency capable of producing continuous and progressive racial changes. Evolution biological as well as geological may still legitimately be regarded as a gradual and continuous process free from sudden catastrophes.

The idea of fixity among living things seems to be one which the human mind is loath to give up and which has to be constantly combated in the advancement of biology. For centuries it was the fixity of species which dominated biological thought. Darwin had to dispel this idea before he could get a hearing for evolution. When the Mendelian theory of unit-characters came in, the idea of fixity, unchangeableness, attached itself to the unit-characters. Driven from this hold,

it now seizes on the single factors on which Mendelian characters depend. Simultaneously it attaches itself to the conjectural mechanism which underlies Mendelian heredity, the chromosomes. We hear much now about their fixity and constancy of structure down to the minutest visible granules, and the argument is even offered that inherited characters must be constant because the chromosomes are. It is probable that, if chromosomes could be seen as readily as inherited characters, their structure would be found to be no more constant than that of the inherited characters supposed to depend upon them. As a matter of fact students of the chromosomes do observe great variability in the size, shape, density and even in the number of the chromosomes, but those who wish to believe in the fixity of such structures find convenient explanations for these observed variations in the action of killing reagents, stains, etc., just as we geneticists invoke supplementary and modifying factors when we desire to defend the idea of fixity in our hypothetical genetic factors. The biologist may well take warning from the history of his science against assuming fixity of either structure or function in living things. The search for fixity will doubtless continue to shift, as it has done heretofore, from higher to lower stages, and will not find what it is looking for until it reaches the inorganic materials which, though they are the building stones of life, are not life itself.

Certain questions will occur to the critical reader. Is the evidence for the foregoing conclusions adequate? Are the conclusions based on a sufficient number of observations, and have these observations been carefully and accurately made? I believe that all these questions may be answered in the affirmative. Seventeen generations of offspring in the minus selection series and sixteen generations in the plus selection series have been studied. The generations of plus or minus selected offspring respectively average over a thousand individuals each, the total for the entire series being 33,249 rats, all descended from less than a dozen original recessive animals whose progeny have been continuously selected in a particular direction without intercrossing between the two series since the experiment began. Of course control crosses of various sorts have been made, as with wild rats, and between the two series, but the derivatives of such crosses have been wholly excluded from the selection series here described. Certainly no such mass of material dealing with the variation in a single Mendelian character has previously been available for study. The grading has been done with the same standard set of grades constantly at hand for comparison, and it has been done mostly by one person. The series of observations has been made possible through financial assistance received from the Carnegie Institution of Washington. Dr. John C. Phillips has rendered valuable assistance in the arduous work of raising and studying the large numbers of animals involved in these experiments.